Subpart W - CFR 158 Antimicrobials Data Requirements

158.1100 General requirements.

(a) This subpart establishes the data requirements for pesticide products that are generally considered to be antimicrobial products, including, but not limited to, wood and materials preservatives, antifouling products, algaecides, disinfectants, sanitizers, and sterilants. Refer to Appendix A which describes the use categories for products covered by this part.

158.1101 Definitions.

Unless explicitly defined in this subpart, terms defined in FIFRA sec 2 and Part 152 of this chapter apply to this subpart.

158.1103 Applicability of data requirements.

(a) Unless otherwise stated in this subpart, subpart A of this part applies to all data submitted for antimicrobial products.

(b) The data requirements in this subpart are not exclusive. If a product bears some uses for which data requirements in this subpart would apply and other uses for which data requirements in subparts D through U would apply, the applicant must satisfy both sets of data requirements. If an applicant is unsure which data requirements apply to his product, he should contact EPA for a determination.

(c) Notwithstanding this subpart, EPA may require additional data on a case-by-case basis in order to conduct a risk assessment for the product. Although this subpart covers most of the data requirements for most use situations, it cannot address all possible individual use situations.

158.1104 How to use data tables.

(a) Data tables. Data tables address requirements for product chemistry, residue chemistry, toxicology, environmental fate, ecological effects, human exposure, and product performance or efficacy data. Each table includes the following information:

(1) The name of the data requirement, e.g., subchronic oral study;

(2) Whether the data are required (R) or conditionally required (CR);

(3) The test substance (manufacturing use product or end use product);

(4) A reference to the EPA Pesticide Assessment Guidelines series which contains the protocols, test standards, evaluation procedures and reporting requirements for the study; and

(5) Notes or conditions attached to the data requirements which clarify the applicability of the data requirements.

(b) Label restrictions. In some use categories, label restrictions or other conditions of use, if followed by the user, would be expected to eliminate or decrease exposure to the pesticide. In this case, some data requirements may no longer apply. Such label restrictions must be practicable by the intended user and, if followed, likely to result in an acceptably lower level of exposure.

158.1105 Data requirements for end use products.

(a) Data on end use formulation. Each end use product must be supported by the data listed in this section. These studies are conducted using the end use product as formulated for sale and distribution. Data from studies as specified in paragraphs (d), (e) and (f), must be submitted in whole, or may be cited in accordance with the data compensation provisions of subpart E of this part,

(b) Data on active ingredient(s). Except as provided in paragraph (c), each end use product must be supported by data on each active ingredient, which depend primarily upon the uses proposed for registration. The data required for active ingredients are specified by use category in Appendix A of this subpart.

(c) Formulators' exemption. The formulator's exemption (see 152.85) relieves applicants for end use registrations of the obligation to submit or cite data on an active ingredient if all of the following are true.

(1) The source of the active ingredient is a registered product.

(2) The product proposed for registration bears only uses included in the registration of the source active ingredient product. If the product proposed for registration bears a use not included in the source active ingredient registration, the applicant must submit or cite data on the active ingredient for those sites or uses not included in the source active ingredient product.

(d) Product chemistry information. The applicant must submit or cite the product chemistry data and information specified in Table 1. The data must be derived from testing using the product as formulated for sale and distribution.

(1) Data and information required in Table 1 must be submitted with the application unless it is in Agency files and is current and accurate.

(2) Studies pertaining to physical and chemical properties of the product in Table 1 may be submitted in full or, in the applicant's discretion, the results may be summarized on a form available from the Agency. In this latter case, the full studies must be maintained by the applicant and submitted upon request.

Table 1. Product chemistry data requirements

Data Requirements	R/CR	Notes, Conditions	Test Substance	Guideline Reference	
				Old	New
~~Product Identity, Composition and Analysis~~					
Product identity and composition	[R]		EP	158.155 (61-1)	830.1550
Description of starting materials	[R]		EP	158.160 (61-2)	830.1600
Description of production process	[R]		EP	158.162 (61-2)	830.1620
Description of formulation process	[R]		EP	158.165 (61-2)	830.1650
Discussion of formation of impurities	[R]		EP	158.167 (61-3)	830.1670
Preliminary analysis	[R]	Required to support the registration of end use products produced by an integrated system. Data on other end-use products will be required on a case-by-case basis.	EP	158.170 (62-1)	830.1700
Certified limits	[R]	Certified limits are not required for inert ingredients in products proposed for experimental use.	EP	158.175 (62-2)	830.1750
Enforcement analytical method	[R]	Required to support the registration of end use products produced by an integrated system. Data on other end-use products will be required on a case-by-case basis.	EP	158.180 (62-3)	830.1800
Submittal of samples	[R]	Samples of end-use products produced by an integrated system are to be submitted on a case-by-case basis. For analysis of the end product, basic manufacturers are required to provide the Agency with a sample of each TGAI when first used as a formulating ingredient in products registered under FIFRA. A sample of the pure active ingredient (PAI) suitable for use as an analytical	EP	64-1	830.1900

Data Requirements	R/CR	Notes, Conditions	Test Substance	Guideline Reference	
				Old	New
		standard is also required at this time.			
~~**Physical/Chemical properties**~~					
Physical state	[R]		EP	63-3	830.6303
Density/relative density/bulk density	[R]	Bulk density must be defined for solid EPs. True density or specific gravity are applicable to other test substances.	EP	63-7	830.7300
pH	[CR]	Required when the test substance is soluble or dispersible in water.	EP	63-12	830.7000
Oxidation/reduction: chemical incompatibility	[CR]	Required when the product contains an oxidizing or reducing agent.	EP	63-14	830.6314
Flammability	[CR]	Required when the product contains combustible liquids.	EP	63-15	830.6315
Explodability	[CR]	Required when the product is potentially explosive.	EP	63-16	830.6316
Storage stability	[CR]	The requirement for data on the EP applies only when: (i) The product use pattern is one for which performance (efficacy) data are required; or (ii) Product instability is suspected or incidents of instability are reported.	EP	63-17	830.6317
Viscosity	[CR]	Required when the product is a liquid.	EP	63-18	830.6318
Miscibility	[CR]	Required when the product is an emulsifiable liquid and is to be diluted with petroleum solvents.	EP	63-19	830.6319
Corrosion characteristics	[R]		EP	63-20	830.6320
Dielectric breakdown voltage	[CR]	Required when the EP is a non-conductant liquid and is expected to be used around electrical equipment.	EP	63-21	830.6321

(e) Acute toxicity data. The applicant must submit or cite the six acute toxicity studies listed in Table 2, conducted using the product as formulated for sale and distribution. If the product is intended and labeled to be diluted for use, the applicant may wish also to conduct certain studies using the highest diluted concentration (lowest dilution rate) permitted by the labeling. Before conducting such studies, an applicant is encouraged to consult the Agency to determine whether calculated values may be used instead of studies on the use dilution.

Table 2. Acute toxicity studies.

Name	R/CR	Note/conditions	Old Guideline Reference Number	New Guideline Reference Number
Acute Oral Toxicity	[R]	Not required if product is a gas or highly volatile liquid.	81-1	870.1100
Acute Dermal Toxicity	[R]	Not required if product is a gas or highly volatile liquid. Not required if product is highly corrosive to skin or has pH < 2 or > 11.5; such a product will be classified as toxicity category I for potential dermal toxicity effects.	81-2	870.1200
Acute Inhalation Toxicity	[R]	Required when product consists of, or under conditions of use will result in, an inhalable material (e.g., gas, vapor or aerosol/particulate).	81-3	870.1300
Acute Eye Irritation	[R]	Not required if product is a gas or highly volatile liquid. Not required if product is highly corrosive to skin or has pH < 2 or > 11.5; such a product will be classified as toxicity category I for potential eye irritation effects.	81-4	870.2400
Acute Dermal Irritation	[R]	Not required if product is a gas or highly volatile liquid. Not required if product is highly corrosive to skin or has pH < 2 or > 11.5; such a product will be classified as toxicity category I for potential dermal irritation effects.	81-5	870.2500
Skin Sensitization	[R]	Required unless repeated dermal exposure does not occur under conditions of use.	81-6	870.2600

(f) Product performance (efficacy) data. The applicant must ensure through testing that his product is, and after registration continues to be, efficacious when used in accordance with label directions and widespread and commonly recognized pest control practices. Efficacy data are developed based upon the product as distributed and sold. The applicant must develop and maintain the relevant data upon which the determination of efficacy is based.

(1) Requirements for antimicrobial products for public health uses.

(i) Scope of public health uses. If the product bears a claim for any public health use, the applicant must submit efficacy data. Products bearing claims to control organisms that may pose a threat to human health, either directly or through transmittal of disease, are considered public health related pesticidess, and require specific efficacy data to support labeling claims and patterns of use. The Agency will use the following criteria to determine whether or not the labeling of an antimicrobial agent bears claims of human health significance.

(A) Products bearing labeling claims to control specific microorganisms directly infectious for man, or indirectly infectious for man (i.e., by transmittal) such as *Escherichia coli, Staphylococcus aureus*, *Mycobacterium tuberculosis*, and *Pseudomonas aeruginosa*, are considered to be directly related to human health.

(B) All sterilizers, disinfectants, swimming pool water disinfectants, human drinking water disinfectants and purifiers, and food-contact surface sanitizers are human health-related, whether or not control of infectious microorganisms is specifically claimed.

(C) Veterinary and animal premise disinfectants are considered human health-related if microorganisms that are infectious for both man and animals are involved, such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*. Microorganisms that are solely pathogenic for animals (such as canine distemper virus, hog cholera virus) are not considered human health-related.

(D) Products intended as disinfectants or sanitizers are considered to include or imply effectiveness against microorganisms infectious for man. Such claims should be expressly qualified in order to remove claims of human health significance (e.g., "disinfects odor-causing bacteria" or "sanitizes slime-forming bacteria"). In addition, if the intent of the claim is not clearly defined, a label disclosure of ineffectiveness of the product against health-related microorganisms may be appropriate (e.g., "The product has not been demonstrated to be effective against microorganisms infectious for man").

The table sets out the efficacy data requirements for public health products. The table specifies, by antimicrobial claim and site, the name and EPA Guideline number of the

study protocol. Applicants are encouraged to consult the Agency before initiating any test for which a protocol is not specified, for example, simulated or in-use tests.

Table 3. Efficacy data requirements for public health products.

Efficacy Level Claimed	**Use pattern**	**Test Required**	**Old Guideline Reference Number**	**New Guideline ReferenceNumber**
STERILANT CLAIM				
	Any site/application uses	AOAC Sporicidal Test	91-2 (a)	810.2100 (b)
DISINFECTANT CLAIM				
	Hard inanimate surfaces	AOAC Use Dilution Test (Hard water and organic soil) **or** AOAC Germicidal Spray Test **or** AOAC Hard Surface Carrier Test (Distilled water only)	91-2 (b), (c), (d)	810.2100 (c), (d), (e)
	Toilet bowl, urinal surfaces	AOAC Use Dilution Test (Hard water and organic soil) **or** AOAC Germicidal Spray Test **or** AOAC Hard Surface Carrier Test (Distilled water only)	91-7 (a)(1)	810.2600 (b)(1)
	Swimming pool, spa, hot tub, jacuzzi, whirlpool water	AOAC method for water disinfectants for swimming pools: Lab test **and** Field in-use test	91-8 (c)	810.2700 (d)
	Human drinking water: emergency water supplies	EPA Guide Standard and Protocol for Testing Microbiological Water Purifiers or Controlled or Simulated In-Use Study	91-8 (a)(2)	810.2700 (b)(1)
	Laundry additives: pre-soak treatment	AOAC Hard Surface Carrier Test (Distilled water only)**or** AOAC Use-Dilution Test Method modified to include organic soil (Hard water)	91-4 (a)(1)	810.2300 (b)(2)
	Laundry additives: (non-residual)	Petrocci and Clarke Laundry Additives (disinfectant level)or actual in-use study	91-4 (a)(2)	810.2300 (b)(3)

Efficacy Level Claimed	Use pattern	Test Required	Old Guideline Reference Number	New Guideline ReferenceNumber
	Presaturated/impregnated towelettes	Simulated in-use study	----	810.2100 (i)
WATER PURIFICATION CLAIM				
	Water treatment units including Emergency water supplies	EPA Guide Standard and Protocol for Testing Microbiological Water Purifiers	91-1 (a)(2), (a)(3), 91-8 (a)(2)	810.2700 (b)(2), (b)(3)
TUBERCULOCIDAL CLAIM				
	Any site/application	**AOAC Tuberculocidal Activity Test Method (standard) or AOAC Tuberculocidal Activity of Disinfectants Test Method (modified) or Quantitative Tuberculocidal Activity Test Method or AOAC Germicidal Spray Products Test (modified for spray products)**	**91-2 (g)**	**810.2100 (h)**
VIRUCIDAL CLAIM IN CONJUNCTION WITH DISINFECTANT CLAIM				
	Any site/application	**Virucidal Activity Method used in conjunction with modifications of: AOAC Hard Surface Carrier Test (Distilled water only) or AOAC Germicidal Spray Test**	**91-2 (f)**	**810.2100 (g)**

Efficacy Level Claimed	Use pattern	Test Required	Old Guideline Reference Number	New Guideline ReferenceNumber
FUNGICIDAL CLAIM				
	Any site/application	AOAC Fungicidal Test or AOAC Hard Surface Carrier Test (Distilled water only) or AOAC Germicidal Spray Products Test	91-2 (c)	810.2100 (f)
SANITIZING CLAIM				
	Non-food contact surfaces (non-residual)	Sanitizer Test for Hard Inanimate Non-food contact surfaces	91-2 (j)	810.2100 (l)
	Previously cleaned food-contact surfaces (non-residual)	Halide chemical products: AOAC Available Chlorine Germicidal Equivalent Concentration Method All other chemical products: AOAC Germicidal and Detergent Sanitizers Method	91-2 (k)(1). (2) 91-2 (l)(2)	810.2100 (m)(1) 810.2100 (m)(2)
	Laundry additives: sanitizing pre-soak	Sanitizer Test for Hard, Inanimate Non-Food Contact Surfaces modified to include organic soil	----	810.2100 (b)(2)
	Laundry additives (non-residual)	Petrocci and Clarke Laundry Additives Method (sanitizing level)	1-4 (a)(3)	810.2300 (b)(4)
	Fabrics and textiles: impregnated self-sanitizing	Simulated in-use study	91-4 (d)	810.2300 (e)
	Carpets	EPA carpet sanitizer protocol	91-4 (b)	810.2300 (c)

Efficacy Level Claimed	Use pattern	Test Required	Old Guideline Reference Number	New Guideline ReferenceNumber
	Air	Glycol-containing: Chemical Analysis Non-glycol-containing: Quantitative Microbiological Assay	91-5 (b)(1) 91-5 (b)(2)	810.2400 (b)(1) 810.2400 (c)(2)
	Toilet bowl and urinal surfaces	Sanitizer Test for Hard Inanimate Non-food Contact Surfaces	91-7 (a)(2)	810.2600 (b)(2)
	Toilet and urinal bowl water	Simulated use study	91-7 (b)(1)	810.2600 (c)(1)
	Toilet in-tank sanitizers	Simulated use study	---	810.2600 (d)(1)
RESIDUAL SELF-SANITIZING CLAIM				
	Hard surfaces (residual self-sanitizing activity of dried chemical residues on hard inanimate surfaces)	Controlled in-use study: or simulated in-use study	91-2 (m)	810.2100 (c)
	Laundry additives: (residual self-sanitizing)	Petrocci and Clark Laundry Additives or AATCC Test Method 100-1974	91-4 (a)(4)	810.2300 (b)(5)
STERILANT, DISINFECTANT, OR SANITIZING CLAIM				
	Mattresses, upholstered furniture, pillows	Simulated in-use test	91-4 (c)	810.2300 (d)

(2) Requirements for antimicrobial products for non-public health uses. If the product bears no claim for any public health use, the applicant must generate efficacy data utilizing the appropriate test method(s) and these data must be kept on file in the applicant's records. However, if EPA does not require the submission of efficacy data on such products, EPA will not make any determination regarding efficacy in the registration process.

(g) Request for submission of data to EPA. A request for submission of required data is not a Data Call-In under FIFRA sec. 3(c)(2)(B). As a condition of registration, EPA requires that such data be made available upon request, either before or after registration. Failure to submit efficacy data when requested may result in the cancellation of registration with only limited hearing rights under FIFRA sec. 6(e).

158.1106 Product chemistry data requirements.

The requirements of subpart D of this part apply to all manufacturing and end use products in all use categories.

158.1107 Efficacy data requirements.

(a) Requirements for antimicrobial agents for public health uses.

(1) Scope of public health uses. Products to control organisms that may pose a threat to human health, either directly or through transmittal of disease, are considered public health related antimicrobials, and require specific efficacy data to support labeling claims and patterns of use. The following criteria for determination of whether the antimicrobial agent bears claims of human health significance are listed in 158.1105 (f)(1).

(2) Data required for public health uses. An applicant for registration of a manufacturing use product intended for public health uses must provide presumptive evidence of its intrinsic value as an antimicrobial agent. An example of the types of presumptive tests acceptable is the Hard Surface Carrier Test. For end use efficacy data requirements, refer to 158.1105 (f).

(3) Data for nonpublic health uses. The Agency has waived all requirements to submit efficacy data for pesticides unless the pesticide product bears a claim to control pest organisms that may pose a threat to human health. However, each applicant and registrant must ensure through testing that his products are efficacious when used in accordance with label directions and commonly accepted pest control practices. The applicant and registrant must

develop and maintain the relevant data upon which the determination of efficacy is based. The Agency reserves the right to require, on a case-by-case basis (e.g. significant new uses or benefits data in case of special reviews), submission of efficacy data for any pesticide product, registered or proposed for registration, when necessary.

158.1108 Residue chemistry data requirements.

(a) General requirements. Residue chemistry data are used by the Agency to estimate the exposure of the general population to pesticide residues in food and for setting and enforcing tolerances for pesticide residues in food or feed.

(1) Food uses.

(i) Indirect food contact. Use of antimicrobial products for food area premises or equipment will generally be considered food uses. Such indirect food contact uses are under Use Category I. Agricultural premises and equipment. Category II. Food handling/storage establishments premises and equipment, and Category IV. Residential and public access premises. With the exception of Category IV, registration must be supported by data sufficient to support establishment of a tolerance or exemption from the requirements of a tolerance under the Federal Food, Drug and Cosmetic Act (FFDCA). The Agency will consider label modifications which clarify practices such that use of the antimicrobial product is unlikely to result in pesticide residues in food. For example, a disinfectant applied to food handling equipment or surfaces will be considered nonfood if the food is covered or removed during application and the treated surfaces are rinsed with potable water prior to any contact with food. In contrast, tolerances or exemptions from the requirements of a tolerance will be required for sanitizing solutions which remain on the surface of food handling or processing equipment.

Antimicrobial sanitizers incorporated into plastic products such as coffee cups or cutting boards intended for contact with food will also require tolerances or tolerance exemptions.

(ii) Direct food contact. Algicides for use in many aquatic areas have the potential to contaminate potable water and would require residue data for tolerance setting purposes.

Antimicrobial products used to treat animal or poulty drinking water or for egg washing or fruit and vegetable rinses are also considered to be direct food uses and thus are subject to FFDCA for tolerances or tolerance exemptions.

(2) Data and information required.

(i) Information on the chemical identity and composition of the pesticide product, and directions for use providing the amounts, frequency and timing of pesticide application, and results of tests on the amount of residues on or in the treated food or feed, are needed to support a finding

as to the magnitude and identity of residues which result in food or animal feed as a consequence of a proposed pesticide usage. Residue chemistry data are also needed to support the adequacy of methods for the enforcement of the tolerance, and to support practicable methods for removing residues that exceed any proposed tolerance.

(ii) For indirect food uses, the Agency uses Directions for Use in combination with historical residue data concerning the amount of sanitizing solution remaining on food contact surfaces and food consumption data to calculate the amount of antimicrobial transferred to the food. If the antimicrobial has sanitizing action and is meant to be embedded in plastic products with food contact uses, the Agency can assume complete transference into food over the lifetime of the plastic product. If toxicology concerns are acute rather than chronic, applicants are required to provide migration studies demonstrating the rate of transference of the antimicrobial into the food.

(iii) Residue chemistry studies include metabolism studies which define the nature of the residue and magnitude of the residue studies which measure how much residue is present in food, feed or water. Most direct food uses require both types of studies, although magnitude of the residue studies may be waived in cases where the residue level can be calculated easily based on the use directions, e.g., uses which specify a certain concentration in human drinking water.

158.1109 Data requirements for residue chemistry.

(a) Table. Section 158.1104 describes how to use the table to determine the data requirements and the substance to be tested. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (b) of this section, and apply to the individual tests when referenced in the use column of the following table.

Table 1. Residue chemistry data requirements.

Data Requirements	Animal Drinking Water	Indirect Food Contact Sanitizers	Egg Washes and Fruit and Vegetable Rinses	Aquatic Outdoor Uses	Test Substance	Guideline Reference
Chemical identity	R 1	R 1	R 1	R 1	TGAI	860.1100
Directions for use	R	R	R	R		860.1200
Migration studies		CR 2			TGAI	none
Nature of the residue - plants or Hydrolysis	R 3		CR 15	R 18	PAIRA	860.1300 or 835.2120
Nature of the residue - livestock	CR 4		CR 16	CR 19	PAIRA or plant metabolite	860.1300
Residue analytical method	R 5,7	CR 6,7	CR 6,7	R 5,6,7	Residue of concern	860.1340
Multiresidue method	R 8	CR 8	CR 8	R 8	Residue of concern	860.1360
Storage stability data	R 9		CR 9	R 9	TEP or residue of concern	860.1380
Processed food/feed			CR 17	CR 17	TEP	860.1520
Meat/milk/poultry/eggs	CR		CR	CR	TGAI or	860.1480

Data Requirements	Animal Drinking Water	Indirect Food Contact Sanitizers	Egg Washes and Fruit and Vegetable Rinses	Aquatic Outdoor Uses	Test Substance	Guideline Reference
	10		23	24	plant metabolite	
Potable water	R 11			CR 20	TEP	860.1400
Fish				R 21	TEP	860.1400
Irrigated crops				CR 22	TEP	860.1400
Anticipated residues	CR 12		CR 12	CR 12	Residue of concern	860.1540
Proposed tolerance	R 13	R 13	R 13	R 13	Residue of concern	860.1550
Reasonable grounds in support of a petition	R 13	R 13	R 13	R 13		860.1560
Submittal of analytical reference standards	R 14	CR 14	R 14	R 14	PAI and residue of concern	860.1650

(b) Test notes.

A. Animal drinking water.

(1) The chemical identity data as required in Subpart C are required, with emphasis on impurities that could constitute a residue problem.

(3) For animal drinking water, a radiolabeled study is required to determine the metabolites and/or degradates in water unless adequate metabolism studies are available for growing plants.

(4) Required for the following types of applications: (1) direct applications to animal drinking water; and (2) applications to any surfaces which will contact drinking water unless treated surfaces are rinsed with potable water prior to introduction of animals, feed and drinking water.

(5) An analytical method capable of measuring residues in water is required.

(7) A residue method suitable for enforcement of tolerances is needed whenever a numeric tolerance is proposed. Exemptions from the requirement of a tolerance may also require an analytical method. New enforcement methods need to be supported by results of an independent laboratory validation as described in PR Notice 96-1, available from the Agency.

(8) For any uses requiring a tolerance, data on whether the FDA/USDA multiresidue methodology would detect and identify the antimicrobial and its metabolites are required.

(9) Required for any food use requiring magnitude of the residue studies unless analytical samples are stored frozen for #30 days and the antimicrobial is not known to be volatile or labile.

(10) For applications to drinking water, a feeding study is required if detectable residues are likely in meat, milk, poultry and/or eggs based on the livestock metabolism studies and residue levels in water.

(11) Required whenever an antimicrobial is to be applied directly to water, unless the use directions are designed to achieve a specific concentration of the pesticide in the water.

(12) When the assumption of tolerance level residues would result in predicted exposure at an unacceptable level, data on the level of residue in food as consumed (anticipated residue) will be used to obtain a more precise estimate of potential dietary exposure.

(13) A petition, supported by reasonable grounds and proposing a numerical tolerance or an exemption from a tolerance, is required for any food use.

(14) An analytical reference standard is required for any food use requiring a tolerance. Material safety data sheets should accompany analytical standards as specified by OSHA in 29 CFR 1910.1200.

B. Sanitizers.

(1) The chemical identity data as required in Subpart C are required, with emphasis on impurities that could constitute a residue problem.

(2) Required or antimicrobials used in plastics for which toxicity concerns are for acute toxicity.

(6) An analytical method capable of measuring residues in foods/feeds is required for any food use.

(7) A residue method suitable for enforcement of tolerances is needed whenever a numeric tolerance is proposed. Exemptions from the requirement of a tolerance may also require an analytical method. New enforcement methods need to be supported by results of an independent laboratory validation as described in PR Notice 96-1, available from the Agency.

(8) For any uses requiring a tolerance, data on whether the FDA/USDA multiresidue methodology would detect and identify the antimicrobial and its metabolites are required.

(13) A petition, supported by reasonable grounds and proposing a numerical tolerance or an exemption from a tolerance, is required for any food use.

(14) An analytical reference standard is required for any food use requiring a tolerance. Material safety data sheets should accompany analytical standards as specified by OSHA in 29 CFR 1910.1200.

C. Egg washes and fruit and vegetable rinses.

(1) The chemical identity data as required in Subpart C are required, with emphasis on impurities that could constitute a residue problem.

(6) An analytical method capable of measuring residues in foods/feeds is required for any food use.

(7) A residue method suitable for enforcement of tolerances is needed whenever a numeric tolerance is proposed. Exemptions from the requirement of a tolerance may also require an analytical method. New enforcement methods need to be supported by results of an independent laboratory validation as described in PR Notice 96-1, available from the Agency.

(8) For any uses requiring a tolerance, data on whether the FDA/USDA multiresidue methodology would detect and identify the antimicrobial and its metabolites are required.

(9) Required for any food use requiring magnitude of the residue studies unless analytical samples are stored frozen for #30 days and the antimicrobial is not known to be volatile or labile.
(12) When the assumption of tolerance level residues would result in predicted exposure at an unacceptable level, data on the level of residue in food as consumed (anticipated residue) will be used to obtain a more precise estimate of potential dietary exposure.

(13) A petition, supported by reasonable grounds and proposing a numerical tolerance or an exemption from a tolerance, is required for any food use.

(14) An analytical reference standard is required for any food use requiring a tolerance. Material safety data sheets should accompany analytical standards as specified by OSHA in 29 CFR 1910.1200.

(15) For indoor food uses a radiolabeled study is required to determine the metabolites and/or degradates in representative foods.

(16) A Nature of the residue study in livestock is required for direct applications to eggs and livestock feeds.

(17) Required if an antimicrobial is used in such a manner that quantifiable residues occur only in the raw agricultural form of a crop and such residues could concentrate upon processing.

(23) For applications to livestock feed, a feeding study is required if detectable residues are likely in meat, milk, poultry and/or eggs based on the livestock metabolism studies and residue levels in feed.

D. Aquatic outdoor uses.

(1) The chemical identity data as required in Subpart C are required, with emphasis on impurities that could constitute a residue problem.

(5) An analytical method capable of measuring residues in water is required.

(6) An analytical method capable of measuring residues in foods/feeds is required for any food use.

(7) A residue method suitable for enforcement of tolerances is needed whenever a numeric tolerance is proposed. Exemptions from the requirement of a tolerance may also require an analytical method. New enforcement methods need to be supported by results of an independent laboratory validation as described in PR Notice 96-1, available from the Agency.

(8) For any uses requiring a tolerance, data on whether the FDA/USDA multiresidue methodology would detect and identify the antimicrobial and its metabolites are required.

(9) Required for any food use requiring magnitude of the residue studies unless analytical samples are stored frozen for #30 days and the antimicrobial is not known to be volatile or labile.

(12) When the assumption of tolerance level residues would result in predicted exposure at an unacceptable level, data on the level of residue in food as consumed (anticipated residue) will be used to obtain a more precise estimate of potential dietary exposure.

(13) A petition, supported by reasonable grounds and proposing a numerical tolerance or an exemption from a tolerance, is required for any food use.

(14) An analytical reference standard is required for any food use requiring a tolerance. Material safety

data sheets should accompany analytical standards as specified by OSHA in 29 CFR 1910.1200.

(17) Required if an antimicrobial is used in such a manner that quantifiable residues occur only in the raw agricultural form of a crop and such residues could concentrate upon processing.

(18) Plant metabolism studies are required to support applications to water since residues could occur in irrigated crops.

(19) A Nature of the residue study is required for applications to aqueous outdoor sites unless it can be determined that the treated water would not eventually be used for drinking purposes by animals.

(20) Required whenever an antimicrobial is to be applied directly to water, unless (1) it can be determined that the treated water would not be used (eventually) for drinking purposes by man or livestock, or (2) the use directions are designed to achieve a specific concentration of the pesticide in the water.

(21) Required for all antimicrobials applied directly to water inhabited by fish.

(22) Required when an antimicrobial is to be applied directly to water that could be used for irrigation or to irrigation facilities such as ditches.

(24) For applications to livestock feed and drinking water, a feeding study is required if detectable residues are likely in meat, milk, poultry and/or eggs based on the livestock metabolism studies and residue levels in feed and water.

158.1110 Toxicology data requirements.

(a) Types of studies. Data required to assess potential hazards to humans and domestic animals are derived from a variety of acute, subchronic, and chronic toxicity studies, as well as assessments of carcinogenicity, developmental toxicity, reproductive effects, mutagenicity, metabolism, immunotoxicity, neurotoxicity, and other special studies.

(1) Acute studies. Acute toxicity studies provide information on the potential for health hazards which may arise as a result of short-term exposure. Results of acute toxicity studies may also suggest the mode of toxic action(s) of the pesticide and assist in the selection of dose levels for other studies.

(2) Subchronic studies. Subchronic studies provide information on health hazards that may result from repeated exposures to a pesticide over a limited period of time. Depending on the most likely route(s) of human exposure, the studies may utilize oral, dermal, or inhalation routes of administration for study durations of up to 90 days. These studies may provide further information on the mode of toxic action(s) of the pesticide, aid in the determination of target organs and systems, allow establishment of dose-response relationships, and indicate the potential for immunotoxic and neurotoxic effects. Subchronic tests assist in the establishment of safety criteria for repeated human exposures over a limited period of time. Subchronic studies (or range-finding studies of at least 90 days duration) should provide information necessary to select proper dose levels for chronic studies and particularly for carcinogenicity studies.

(3) Chronic studies. Information derived from chronic studies is used to assess potential hazards resulting from prolonged and repeated exposures to a pesticide over a significant portion of the human life span. These studies, which are usually conducted by feeding the test material to several mammalian species for periods of 12 to 24 months or longer, are intended to detect toxic effects which may occur after long-term exposure.

(4) Developmental toxicity and reproduction studies. Developmental toxicity studies are designed to assess the potential of the test substance to induce developmental effects in offspring as the result of exposure of the mother during pregnancy. These developmental effects include death of the developing organism, structural abnormalities, altered growth, and functional deficiencies. Functional deficiencies (e.g. developmental neurotoxicity) are generally best assessed in postnatal developmental toxicity studies. Multigeneration reproduction studies are designed to provide information concerning the general effects of a test substance on overall reproductive capability including those effects on gonadal function, estrous cycles, sperm parameters, mating behavior, conception, parturition, lactation, weaning, and growth and development of offspring. This study may also provide information about the effects of the test substance on neonatal morbidity and mortality, and preliminary data on developmental toxicity.

(5) Mutagenicity. An initial battery of mutagenicity tests with possible confirmatory testing is minimally required. In addition, other tests for mutagenicity that may have been performed and as complete a reference list as possible shall be submitted. Subsequent testing may or may

not be required based on the evidence available to the Office of Pesticide Programs in accordance with the objective and considerations for mutagenicity testing. For chemicals designed to kill bacteria, bacterial testing may not be appropriate. However, in keeping with the recommendations of the FIFRA Scientific Advisory Panel, a minimum of three tests would still be required. In this case, the Salmonella typhimurium test should be replaced with an in vitro test for gene mutation in mammalian cells, preferably the mouse lymphoma test. An in vitro cytogenetics test and an in vivo cytogenetics test would comprise the balance of the test battery. Specific choice of assays should be discussed with the Agency.

(6) Metabolism studies. Data from studies on the absorption, distribution, bioaccumulation, excretion, and metabolism of a pesticide may aid in the design of more relevant toxicology studies, allow more meaningful evaluation of test results, and more appropriate risk assessment as a result of more meaningful extrapolation of data on animals to man. More flexibility is needed in the design and conduct of metabolism studies than in most other types of studies to make them useful to the toxicological assessment and to the design of other appropriate toxicology studies. The design of the study may depend on such obvious factors as the physical/chemical characteristics of the pesticide being investigated or on more subtle factors. In some cases, the toxicological effects may be unique to the species tested.

(7) Neurotoxicity studies. Neurotoxicity studies are required to evaluate the potential of each test substance to adversely affect the structure/functions of the nervous system. The objectives of the acute and 90 day studies are to detect and characterize effects on the incidence and severity of clinical signs, the level of motor activity, and histopathology of the nervous system following acute and subchronic exposures. Special neurotoxicity studies such as visual system studies, schedule controlled operant behavior and peripheral nerve function may also be required on a case-by-case basis based on data from screening studies or data on certain chemical classes. Neurotoxic effects in organisms exposed prior to birth or weaning would be tested in the postnatal developmental toxicity study. Results from these studies may be used for qualitative and/or quantitative risk assessment.

(8) Immunotoxicity studies. Immunotoxicity testing is required to evaluate the potential of each test substance to produce adverse suppressive effects on the immune system. A screening approach is utilized consisting of additional immunological endpoints incorporated into otherwise required subchronic, chronic and reproductive studies in rodents. Alternatively, an equivalent independent study may be performed. If warranted by results of this initial testing, additional immunotoxicity studies may be required on a case-by-case basis for qualitative and/or quantitative risk assessment.

(b) Tiered progression. The toxicology test requirements for this category are set out in tiers. Tier one lists data which are generally required. Data required in Tier two are needed to refine risk assessments using the results of tests in tier one in conjunction with human exposure data. The special testing category contains studies required to assess developmental neurotoxicity or metabolism, if warranted by the toxic characteristics of the chemical.

(1) Data required for nonfood and sanitizer uses. Registrants are required to submit a limited first tier of toxicological data with human (applicator) exposure data for Agency review of nonfood antimicrobial uses. For sanitizers, dietary exposure information is required (see 158.1110 (a) Residue chemistry data requirements). The first tier of toxicology data consists of acute toxicity, one or more subchronic studies (depending on route of exposure), acute and subchronic neurotoxicity screening batteries in the rat, one developmental toxicity study, an immunization study, and mutagenicity study. Agency review of potential risk based on first-tier toxicological studies and exposure data allows a determination to be made for the need, if any, for higher tier toxicological studies.

(2) Data required for high exposure uses. Human or animal drinking water, swimming pools, and outdoor aquatic uses in lakes, rivers or streams are considered to be high impact use sites for antimicrobials. The full food use battery of toxicology tests is required at Tier I for these use sites. The battery consists of acute studies, one or more subchronic studies, mutagenicity studies, acute and subchronic neurotoxicity screening batteries, an immunotoxicity study, two developmental toxicity studies, a two-generation reproductive study, and chronic and oncogenicity studies in two species.

158.1111 Data requirements for toxicology.

(a) Table. Section 158.1104 describes how to use this table to determine the toxicology data requirements and the substance to be tested. Specific conditions, qualifications, or exceptions to the designated test procedures appear in the third column of each of the following tables.

Table 1. Toxicology data requirements for nonfood and sanitizing uses.

Data Requirements	R/CR	Notes, Conditions	Test Substance	Guideline Reference	
				Old	New
Tier One					
Acute oral toxicity - rat	R	Not required if test material is a gas or highly volatile liquid.	MP and TGAI	81-1	870.1100
Acute dermal toxicity	R	Not required if test material is a gas or highly volatile liquid. Not required if test material is corrosive to skin or has pH < 2 or > 11.5; such a product will be classified as toxicity category I on the basis of potential dermal toxicity.	MP and TGAI	81-2	870.1200
Acute inhalation toxicity - rat	R	Required when the product consists of, or under conditions of use will result in, an inhalable material (e.g., gas. vapor, or aerosol/particulate).	MP and TGAI	81-3	870.1300
Primary eye irritation - rabbit	R	Not required if test material is corrosive to skin or has pH < 2 or > 11.5; such a product will be classified as toxicity category I on the basis of potential eye irritation effects.	MP	81-4	870.2400
Primary dermal irritation	R	Not required if test material is a gas or highly volatile liquid. Not required if test material is corrosive to skin or has pH < 2 or > 11.5; such a product will be classified as toxicity category I on the basis of potential eye, dermal toxicity, and dermal irritation effects.	MP	81-5	870.2500
Dermal sensitization	R	Required unless repeated dermal exposure does not occur under conditions of use.	MP	81-6	870.2600
Acute neurotoxicity - rat	R	The route of exposure should correspond to a primary route of human exposure.	TGAI	81-8	870.6200
90-Day dermal	R	The 90-day dermal study is required for nonfood uses. For food uses, the requirement for dermal testing may be satisfied by a 28-day dermal study. The EP shall also be tested if any component of the EP may increase	TGAI	82-3	870.3250

Data Requirements	R/CR	Notes, Conditions	Test Substance	Guideline Reference	
				Old	New
		dermal absorption of the active ingredient(s) or potentiate toxic or pharmacologic effects.			
90-Day oral - rodent	CR	Required for food uses.	TGAI	82-1	870.3100
90-Day oral - nonrodent	CR	The nonrodent study is required only when a tolerance or an exemption from the requirements of a tolerance is required.	TGAI	82-1	870.3100
90-Day inhalation - rat	CR	Required if the active ingredient is a gas at room temperature or if the Agency determines that use of the product may result in repeated inhalation exposure at a concentration likely to be toxic regardless of whether the major route of exposure is inhalation.	TGAI	82-4	870.3465
Developmental toxicity - one species	R	The test substance or vehicle is usually administered orally, by oral intubation.	TGAI	83-3	870.3700
Salmonella typhimurium - reverse mutation assay	R	For chemicals designed to kill bacteria, a reverse mutation assay may be performed in mouse lymphoma L5178Y cells in culture.	TGAI	Subdivision F, App. 9	870.5265
Mammalian cells in culture	R	Choice of assays using either mouse lymphoma L5178Y cell thymidine kinase (tk) gene locus, maximizing assay conditions for small colony expression and detection; Chinese hamster ovary (CHO) or Chinese hamster lung fibroblast (v79) cells, hypoxanthine-guanine phosphoribosyl transferase (hgprt) gene locus, accompanied by an appropriate *in vitro* test for clastogenicity; or CHO cells strains AS52, xanthine-guanine phosphoribosyl transferase (xprt) gene locus. For chemicals designed to kill bacteria, since the mouse lymphoma L5178Y test is used as a replacement for the Salmonella typhimurium test, and Advisory Panel, an appropriate in vitro mammalian test should be performed for clastogenicity.	TGAI	Subdivision F, App. 9	870.5300
In vivo cytogenetics	R	Choice of assays, initial considerations usually given to rodent bone marrow, using either metaphase analysis (aberrations) or micronucleus assay.	TGAI	Subdivision F,	870.5380, 870.5385, 870.5395

Data Requirements	R/CR	Notes, Conditions	Test Substance	Guideline Reference	
				Old	New
				App. 9	870.5395
Immunotoxicity	R	All 90-day subchronic studies in rats can be designed to simultaneously fulfill the requirements of the immunotoxicity study.	TGAI	85-7	870.7800
90-Day neurotoxicity	R	All 90-day subchronic studies in rats can be designed to simultaneously fulfill the requirements of the 90-day neurotoxicity study.	TGAI	82-7	870.6200
Tier Two					
Developmental toxicity - second species	CR	Testing in two species is required if significant exposure of human females of child-bearing age may reasonably be expected. Testing in a second species is required if significant developmental toxicity is observed after testing in the first species. The test substance or vehicle is usually administered orally unless the chemical or physical characteristics of the test substance or pattern of human exposure suggest a more appropriate route of administration (e.g., dermal).	TGAI	83-3	870.3700
Dermal penetration	CR	Required for compounds for which a human risk assessment for dermal exposure is required based on a toxic effect identified by an oral or inhalation study. A risk assessment assuming 100% dermal absorption will be performed to determine if the study is required and to identify the dose(s) and duration(s) of exposure for which dermal absorption must be quantitated.	Choice	85-3	870.7600
Chronic feeding - two species, rodent and nonrodent	CR	Required if use of the pesticide is likely to result in significant human exposure over a substantial portion of the human life span in terms of the frequency, magnitude or duration of exposure.	TGAI	83-1	870.4100
Carcinogenicity - two species, rat and mouse	CR	Required if any of the following criteria are met: (i) The weight of evidence indicates carcinogenic potential of the active ingredient or any of its metabolites, degradation products or	TGAI	83-2	870.4200

Data Requirements	R/CR	Notes, Conditions	Test Substance	Guideline Reference	
				Old	New
preferred		impurities based upon consideration of whether the substance: (A) is structurally related to a recognized carcinogen. (B) causes mutagenic effects as demonstrated by *in vitro* or *in vivo* testing. (C) produces a morphologic effect in any organ (e.g., hyperplasia, metaplasia) in subchronic studies that may lead to neoplastic change. (ii) Use of the pesticide product is likely to result in human exposure over a substantial portion of the human life span which is significant in terms of the frequency, magnitude, or duration of exposure.			
Reproduction	CR	May be required if adverse effects on organs of the reproductive system are observed in 90-day or other studies, or if developmental toxicity is demonstrated in available data. Required if use of the product is likely to result in human exposure over a substantial portion of the human life span which is significant in terms of the frequency, magnitude, or duration of exposure.	TGAI	83-4	870.3800
~~**Special Testing**~~					
Postnatal development toxicity	CR	Required in order to more fully assess any of the manifestations of developmental toxicity or neurotoxicity.	TGAI	83-6	870.6300
General metabolism	CR	Required when chronic and/or carcinogenicity studies are required. Also may be required if significant adverse effects are observed in available toxicology studies (e.g., reproduction and developmental toxicity).	PAI or PAIRA	85-1	870.7485

Table 2. Toxicology data requirements for high exposure uses (Human drinking water, swimming pools, aquatic outdoor, animal drinking water).

Data Requirements	R/CR	Notes, Conditions	Test Substance	Guideline Reference	
				Old	New
Tier One					
Acute oral toxicity - rat	R	Not required if test material is a gas or highly volatile liquid.	MP and TGAI	81-1	870.1100
Acute dermal toxicity	R	Not required if test material is a gas or highly volatile liquid. Not required if test material is corrosive to skin or has pH < 2 or > 11.5; such a product will be classified as toxicity category I on the basis of potential dermal toxicity.	MP and TGAI	81-2	870.1200
Acute inhalation toxicity - rat	R	Required when the product consists of, or under conditions of use will result in, an inhalable material (e.g., gas. vapor, or aerosol/particulate).	MP and TGAI	81-3	870.1300
Primary eye irritation - rabbit	R	Not required if test material is corrosive to skin or has pH < 2 or > 11.5; such a product will be classified as toxicity category I on the basis of potential eye irritation effects.	MP	81-4	870.2400
Primary dermal irritation	R	Not required if test material is a gas or highly volatile liquid. Not required if test material is corrosive to skin or has pH < 2 or > 11.5; such a product will be classified as toxicity category I on the basis of potential eye, dermal toxicity, and dermal irritation effects.	MP	81-5	870.2500
Dermal sensitization	R	Required unless repeated dermal exposure does not occur under conditions of use.	MP	81-6	870.2600
Acute neurotoxicity - rat	R	The route of exposure should correspond to a primary route of human exposure.	TGAI	81-8	870.6200
90-Day oral - rodent	R	Required for all high exposure uses.	TGAI	82-1	870.3100
90-Day oral - nonrodent	CR	Required for human drinking water uses or when a tolerance or an	TGAI	82-1	870.3150`

Data Requirements	R/CR	Notes, Conditions	Test Substance	Guideline Reference	
				Old	New
		exemption from the requirements of a tolerance is required.			
90-Day dermal	R	The 90-Day dermal study is required for nonfood uses. The requirement for dermal testing may be satisfied by a 28-Day dermal study. The EP shall also be tested if any component of the EP may increase dermal absorption of the active ingredient(s) or potentiate toxic or pharmacologic effects.	TGAI	82-3	870.3250
90-Day inhalation - rat	CR	Required if the active ingredient is a gas at room temperature or if the Agency determines that use of the product may result in repeated inhalation exposure at a concentration likely to be toxic regardless of whether the major route of exposure is inhalation.	TGAI	82-4	870.3465
Developmental toxicity - two species	R	The test substance should be administered orally, by oral intubation.	TGAI	83-3	870.3700
Salmonella typhimurium - reverse mutation assay	R	For chemicals designed to kill bacteria, a reverse mutation assay may be performed in mouse lymphoma L5178Y cells in culture.	TGAI	Subdivision F, App. 9	870.5265
Mammalian cells in culture	R	Choice of assays using either mouse lymphoma L5178Y cell thymidine kinase (tk) gene locus, maximizing assay conditions for small colony expression and detection; Chinese hamster ovary (CHO) or Chinese hamster lung fibroblast (v79) cells, hypoxanthine-guanine phosphoribosyl transferase (hgprt) gene locus, accompanied by an appropriate *in vitro* test for clastogenicity; or CHO cells strains AS52, xanthine-guanine phosphoribosyl transferase (xprt) gene locus. For chemicals designed to kill bacteria, since the mouse lymphoma L5178Y test is used as a replacement for the Salmonella typhimurium test, and an appropriate in vitro mammalian test should be performed for clastogenicity.	TGAI	Subdivision F, App. 9	870.5300
In vivo cytogenetics	R	Choice of assays, initial considerations usually given to rodent bone marrow, using either metaphase analysis (aberrations) or micronucleus	TGAI	Subdivision F, App. 9	870.5380, 870.5385,

Data Requirements	R/CR	Notes, Conditions	Test Substance	Guideline Reference	
				Old	New
		assay.		App. 9	870.5395
Immunotoxicity	R	All 90-day subchronic studies in rats can be designed to simultaneously fulfill the requirements of the immunotoxicity study.	TGAI	85-7	870.7800
90-Day neurotoxicity	R	All 90-day subchronic studies in rats can be designed to simultaneously fulfill the requirements of the 90-day neurotoxicity study.	TGAI	82-7	870.6200
Chronic feeding - two species, rodent and non-rodent	R		TGAI	83-1	870.4100
Carcinogenicity - two species, rat and mouse preferred	R		TGAI	83-2	870.4200
Reproduction	R		TGAI	83-4	870.3800
~~**Tier two**~~					
Developmental toxicity - dermal	CR	When a pesticide is determined to be a developmental toxicant (e.g., after oral dosing) and dermal exposure is significant, additional testing via the dermal route may be required.	TGAI	83-3	870.3700
Dermal penetration	CR	Required for compounds for which a human risk assessment for dermal exposure is required based on a toxic effect identified by an oral or inhalation study. A risk assessment assuming 100% dermal absorption will be performed to determine if the study is required and to identify the dose(s) and duration(s) of exposure for which dermal absorption must be quantitated.	Choice	85-3	870.7600
~~**Special Testing**~~					

Data Requirements	R/CR	Notes, Conditions	Test Substance	Guideline Reference	
				Old	New
Postnatal development toxicity	CR	Required in order to more fully assess any of the manifestations of developmental toxicity or neurotoxicity.	TGAI	83-6	870.6300
General metabolism	R		PAI or PAIRA	85-1	870.7485

158.1112 Terrestrial and aquatic nontarget organisms data requirements.

(a) General requirements. The information required to assess hazards to nontarget organisms is derived from tests to determine pesticidal effects on birds, mammals, fish, aquatic invertebrates, bees and nontarget plants These tests include short-term acute, subacute, reproduction, and field studies arranged in a hierarchical or tier system. The results of each tier of tests must be evaluated to determine the potential of the pesticide to cause adverse effects, and to determine whether further testing is required. A purpose common to all data requirements is to provide data which determine the need for (and appropriate wording for) precautionary label statements to minimize the potential adverse effects to nontarget organisms.

(b) Short-term studies. The short-term acute laboratory studies provide basic toxicity information which serves as a starting point for the hazard assessment. These data are used to establish acute toxicity levels of the active ingredient to the test organisms; to compare toxicity information with measured or estimated pesticide residues in the environment in order to assess potential impacts on plants; and to indicate whether further laboratory and/or field studies are needed.

(c) Field studies. Additional studies (i.e. simulated field and full field studies) may be required when basic data and environmental conditions suggest possible problems.

158.1113 Data requirements for terrestrial and aquatic nontarget organisms.

(a) Table. Section 158.1104 describes how to use this table to determine the terrestrial and aquatic nontarget organisms data requirements and the substance to be tested. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (b) of this section, and apply to the individual tests when referenced in the following table.

Table 1. Ecological effects data requirements.

Data Requirements	**Indoor** Agricultural; Food Handling; Commercial; Residential; Medical; Human Drinking Water; Materials Preservatives; Swimming Pools	**Aquatic Industrial** Industrial Processes and Water Systems Group A	Group B	**Antifoulants** Antifouling Coatings	**Wood Preservatives** Wood Preservatives	**Aquatic Outdoor** Aquatic Areas	**Test Substance**	**Guideline Reference** Old	New
Acute EC50 freshwater invertebrates (preferably Daphnia)	R 1	R	[R] 5	R	R	[R]	TGAI, TEP	72-2	850.1010
Acute LC50/EC50 estuarine and marine organisms		CR 6	CR 7	R	R 14,15	CR 21	TGAI. TEP	72-3	850.1025, 850.1035, 850.1045, 850.1055. 850.1075
Freshwater fish LC50 (preferably rainbow trout and bluegill)	R 1,2	R	[R] 4	R	R 24	[R]	TGAI, TEP	72-1	850.1075
Fish early life stage and aquatic invertebrate life cycle			R	R 8	CR 14,16,17	[R]	TGAI	72-4	850.1300

Data Requirements	**Indoor** Agricultural; Food Handling; Commercial; Residential; Medical; Human Drinking Water; Materials Preservatives; Swimming Pools	**Aquatic Industrial** Industrial Processes and Water Systems Group A	Group B	**Antifoulants** Antifouling Coatings	**Wood Preservatives** Wood Preservatives	**Aquatic Outdoor** Aquatic Areas	**Test Substance**	**Guideline Reference** Old	New
Fish life cycle			R	CR 9	CR 14,9	R 22	TGAI	72-5	850.1500
Aquatic organism bioavailability/ biomagnification/ toxicity tests			CR 3	CR 3	CR 14,18	CR 3	TGAI	72-6	850.1710, 850.1730. 850.1850
Whole sediment, Acute invertebrates, freshwater			CR 23	R	CR 14,23	[CR] 23	TGAI, TEP	73-1	850.1735
Whole sediment, Acute invertebrates, marine			CR 23	R	CR 14,23	[CR] 23	TGAI, TEP	73-2	850.1740
Simulated or actual field testing for aquatic organisms			CR 3	CR 11	CR 3,14	CR 3	TEP	72-7	850.1950
Avian oral LD50	R	R	R	R	R	[R]	TGAI	71-1	850.2100

Data Requirements	**Indoor** Agricultural; Food Handling; Commercial; Residential; Medical; Human Drinking Water; Materials Preservatives; Swimming Pools	**Aquatic Industrial** Industrial Processes and Water Systems Group A	Group B	**Antifoulants** Antifouling Coatings	**Wood Preservatives** Wood Preservatives	**Aquatic Outdoor** Aquatic Areas	**Test Substance**	**Guideline Reference** Old	New
(preferably mallard or bobwhite	1	1	1		13	1,20			
Avian dietary LC50 (preferably mallard and bobwhite)			CR 3		CR 3,14	[R] 1	TGAI	71-2	850.2200
Seedling emergence - dose response				R 10	CR	R	TEP	123-1	850.4225
Vegetative vigor - dose response					CR 10,14,19	R	TEP	123-1	850.4250
Aquatic plant growth (algal and aquatic plant toxicity) - **[Tiers I and II]**			R	R	CR 14,19	R	TEP or TGAI	123-2	840.4400, 840.5400
Acute pore water fish and			CR 23	CR 23	CR 14,23	[CR] 23	TGAI, TEP	73-3	none

Data Requirements	**Indoor** Agricultural; Food Handling; Commercial; Residential; Medical; Human Drinking Water; Materials Preservatives; Swimming Pools	**Aquatic Industrial** Industrial Processes and Water Systems Group A	Group B	**Antifoulants** Antifouling Coatings	**Wood Preservatives** Wood Preservatives	**Aquatic Outdoor** Aquatic Areas	**Test Substance**	**Guideline Reference** Old	New
invertebrates									
Whole sediment chronic invertebrates			CR 12	CR 12	CR 14,12	CR 12	TGAI, TEP	74-1	none

(b) Test notes.

A.Indoor uses (Agricultural; Food Handling; Commercial; Residential; Medical; Human Drinking Water; Materials Preservatives; Swimming Pools).

(1) Data are generally not required to support end use products of a gas, highly volatile liquid, highly reactive solid, or a highly corrosive material.

(2) Data are generally required on only one species. Testing in two fish species is required for stable chemicals with high volume effluents (for example, but not limited to egg washing, fruit and vegetable rinses, swimming pools, or materials preservatives with high volumes of aqueous effluents) if the LC50 in the first species is >1 ppm.

B. Aquatic industrial and water systems uses.

(1) Data are generally not required to support end use products of a gas, highly volatile liquid, highly reactive solid, or a highly corrosive material.

(3) May be required on a case-by-case basis depending on the results of lower tier ecological studies and pertinent environmental characteristics.

(4) Required when the end use product will be introduced directly into an aquatic environment (e.g., once-through cooling systems).

(5) Data are required for products used in oil and gas operations that are in and around an estuarine or marine environment.

(6) Required when the end use product will be introduced directly into an aquatic environment and when effluent containing product is discharged into estuaries.

(7) Data are required when effluent containing product is discharged into estuaries.

(8) Required for this use pattern unless LC50 and EC50 values determined in acute testing are all greater than 0.01 and the pesticide does persist and bioaccumulate.

(12) Required when mortality exceeds 20% in any concentration level used in acute sediment testing.

(23) Required only for uses in estuarine and marine environments. Sediment toxicity testing is required if a pesticide meets any of the following conditions:

- -Solubility less than or equal to 0.1 mg/L,
- -Koc > 1,000 (or log Koc less than or equal to 4.0),
- -Kd greater than or equal to 50,
- -The pesticide persists in sediments with a half-life > 10 days,
- -Concentration in the interstitial water is equivalent to concentrations known to be toxic in the water column.

C. Antifoulant uses.

(3) May be required on a case-by-case basis depending on the results of lower tier ecological studies and pertinent environmental characteristics.

(8) Required for this use pattern unless LC50 and EC50 values determined in acute testing are all greater than 0.01 mg/L and the pesticide does persist and bioaccumulate.

(9) Required:

(i) If the estimated environmental concentration is greater than or equal to 0.1 of the no-observed-effect level in the fish early life stage or invertebrate life cycle test.

(ii) If studies of other organisms indicate that the reproductive physiology of fish may be affected.

(10) Only one plant species (rice, *Oryza sativa*) must be tested.

(11) May be required on a case-by-case basis depending on the results of lower tier ecological studies and pertinent environmental fate characteristics (can be done in conjunction with monitoring).

(12) Required when mortality exceeds 20% in any concentration level used in acute sediment testing.

(23) Required only for uses in estuarine and marine environments. Sediment toxicity testing is required if a pesticide meets any of the following conditions:

-Solubility less than or equal to 0.1 mg/L,
-Koc > 1,000 (or log Koc less than or equal to 4.0),
-Kd greater than or equal to 50,
-The pesticide persists in sediments with a half-life > 10 days,
-Concentration in the interstitial water is equivalent to concentrations known to be toxic in the water column.

D. Wood Preservatives Uses.

(3) May be required on a case-by-case basis depending on the results of lower tier ecological studies and pertinent environmental characteristics.

(10) Only one plant species (rice, *Oryza sativa*) must be tested.

(12) Required when mortality exceeds 20% in any concentration level used in acute sediment testing.

(13) Data are generally not required to support end use products unless the end products are highly corrosive materials.

(14) Not required for Ready-to-Use wood preservatives.

(15) Required for use on wood that may be used in estuarine and/or marine environments. (Heavy duty uses).

(16) Data are required if treated wood will be used in aquatic sites and any one or more of the following conditions apply:
(i) If any LC50 or EC50 value determined in acute toxicity testing is less than 1 mg/L.
(ii) If the estimated environmental concentration in water is greater than or equal to 0.01 of any EC50 or LC50 determined in acute toxicity testing.
(iii) If the actual or estimated environmental concentration in water is less than 0.01 of any EC50 or LC50 determined in acute toxicity testing and any of the following conditions exist:

(A) Studies of other organisms indicate the reproductive physiology of fish/invertebrates may be affected.

(B) Physicochemical properties indicate cumulative effects may occur.

(C) The pesticide is persistent in water.

(17) Tests must be performed on the most sensitive organism (freshwater or marine).

(18) May be required on a case-by-case basis depending on the results of the Fish Early Life Stage study and pertinent environmental fate characteristics if aquatic exposure from treated wood is likely and the use in aquatic environments is not prohibited.

(19) May be required if aquatic exposure from treated wood is likely and the use in aquatic environments is not prohibited.

(23) Required only for uses in estuarine and marine environments. Sediment toxicity testing is required if a pesticide meets any of the following conditions:

-Solubility less than or equal to 0.1 mg/L,
-Koc > 1,000 (or log Koc less than or equal to 4.0),
-Kd greater than or equal to 50,
-The pesticide persists in sediments with a half-life > 10 days,
-Concentration in the interstitial water is equivalent to concentrations known to be toxic in the water column.

(24) Testing in two species is required for heavy duty wood preservatives. For ready-to-use products, data are required in only one species.

E. Aquatic Outdoor Uses.

(1) Data are generally not required to support end use products of a gas, highly volatile liquid, highly reactive solid, or a highly corrosive material.

(3) May be required on a case-by-case basis depending on the results of lower tier ecological studies and pertinent environmental characteristics.

(12) Required when mortality exceeds 20% in any concentration level used in acute sediment testing.

(20) For outdoor use products that are formulated as granulars, pellets, or baits, avian acute oral LD50 is required when the LD50 of the technical material is less than or equal to 50 mg/kg.

(21) Required if the maximum expected environmental concentration (MEEC) or the estimated environmental concentration (EEC) in the aquatic environment is greater than or equal to one-half of the LC50 or EC50 of the technical grade of the active ingredient when the end use pesticide is used as directed.
The TEP must be tested when any ingredient in the end use formulation other than the active ingredient is expected to enhance the toxicity of the active ingredient or to cause toxicity to aquatic organisms.

(22) May be required on a case-by-case basis depending on the results of the Fish Early Life Stage study and pertinent environmental fate characteristics.

(23) Required only for uses in estuarine and marine environments. Sediment toxicity testing is required if a pesticide meets any of the following conditions:

- Solubility less than or equal to 0.1 mg/L,
- Koc > 1,000 (or log Koc less than or equal to 4.0),
- Kd greater than or equal to 50,
- The pesticide persists in sediments with a half-life > 10 days,
- Concentration in the interstitial water is equivalent to concentrations known to be toxic in the water column.

158.1114 Environmental fate data requirements.

158.1115 General requirements. Individual laboratory environmental fate studies under controlled conditions are required to determine general information without respect to a specific use site on the rates of pesticide degradation, the identities and rates of formation and decline of volatile and nonvolatile degradates, the accumulation of pesticides and their degradates in the ecosystem, and the physical mobility of pesticides and their degradates in the environment.

(a) Table. Section 158.1104 describes how to use the table to determine the environmental fate data requirements and the substance to be tested. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (b) of this section, and apply to the individual tests when referenced in the following table.

Table 1. Environmental fate data requirements.

Data Requirements	**Indoor** Agricultural; Food Handling; Commercial; Residential; Medical; Human drinking Water; Materials Preservatives; Swimming pools	**Aquatic Industrial** Industrial Processes and Water Systems Group A	Group B	**Antifoulants** Antifouling Coatings	**Wood** Preservatives Wood Preservatives	**Aquatic Outdoor** Aquatic Areas	**Test Substance**	**Guideline Reference** Old	New
Use profile		R	R					none	none
Hydrolysis	R	R	R	R 5	R	[R]	TGAI/ PAIRA	161-1	835.2120
Photodegrada-tion in water			CR 1,12	CR 2,12	CR 7,12	R 12	TGAI/ PAIRA	161-2	835.2240
Special leaching study				R	R 8		TEP	none	none
Adsorption/ desorption			CR 1	CR 2,3	CR 7	R	TGAI/ PAIRA	163-1	835.1230
Soil column leaching					CR 11		TGAI/ PAIRA	163-1	835.1240
Accumulation studies in fish (fish BCF)			CR 1	CR 4	CR 7	[CR] 9	TGAI/ PAIRA	165-4	850.1730
Accumulation				CR	CR	[CR]	TEP	165-5	850.1950

Data Requirements	**Indoor** Agricultural; Food Handling; Commercial; Residential; Medical; Human drinking Water; Materials Preservatives; Swimming pools	**Aquatic Industrial** Industrial Processes and Water Systems Group A	Group B	**Antifoulants** Antifouling Coatings	**Wood** Preservatives Wood Preservatives	**Aquatic Outdoor** Aquatic Areas	**Test Substance**	**Guideline Reference** Old	New
studies in aquatic nontarget organisms				3,4	7	10			
Aerobic soil metabolism			CR		CR 11		TGAI/ PAIRA	162-1	835.4100
Anaerobic soil metabolism					CR 11		TGAI/ PAIRA	162-2	835.4200
Aerobic aquatic metabolism			CR 1	CR 2,3	CR 7	[R]	TGAI/ PAIRA	162-4	835.4300
Anaerobic aquatic metabolism			CR 1	CR 2,3	CR 7	R	TGAI/ PAIRA	162-3	835.4400
Aquatic field study						R	TEP	164-2	840.1100
Monitoring of representative U.S. waters				CR 6			TEP	none	none

(b) Test notes.

A. Indoor uses (Agricultural; Food Handling; Commercial; Residential; Medical; Human Drinking Water; Materials Preservatives; Swimming Pools).

None

B. Aquatic industrial processes.

(1) The study may be required if the exposure estimates from the dilution factor model show significant concentration of chemical immediately downstream from the discharge site that may raise toxicity concerns.

(12) Not required if the active ingredient or any of its hydrolytic products do not show absorption or tailing between 290 and 800 Fm.

C. Antifouling coatings.

(2) The study may be required if the exposure estimates from the antifoulant Special Leaching study show significant concentration of the active ingredient and/or its principal degradation products in the aquatic environment that may raise toxicity concerns.

(3) The environmental media (soil, water, hydrosoil, and biota) to be utilized must be collected from the potential impact areas.

(4) The study is required if significant concentration of the active ingredient and/or its principal degradation products are likely to persist in aquatic environment and may accumulate in aquatic organisms (Kow $ 1000 or hydrolysis half-life > 5 days).

(5) Sterile buffered distilled water and sterile synthetic seawater must be used for the antifoulant Special Leaching study.

(6) Required for active ingredients that are highly toxic and persistent in the aquatic environment.

(12) Not required if the active ingredient or any of its hydrolytic products do not show absorption or tailing between 290 and 800 Fm.

D. Wood preservatives.

(7) May be required if exposure estimates from the Special Leaching Study show significant concentration of the active ingredient and/or its principal degradation products in the aquatic environment that may raise toxicity concerns and the active ingredient will be used on wood intended for use in the aquatic environment.

(8) Applicants should discuss protocols before initiating testing.

(11) The study may be required if the exposure estimates from the Special Leaching Study show the potential for significant concentration of the active ingredient and/or its principal degradation products in soil for pressure treated lumber intended for use in contact with soil and that may lead to uptake by food plants.

(12) Not required if the active ingredient or any of its hydrolytic products do not show absorption or tailing between 290 and 800 Fm.

E. Aquatic areas.

(9) Required if significant concentration of the active ingredient and/or its principal degradation products are likely to occur in aquatic environments and may accumulate in aquatic organisms (Kow $ 1000).

(10) Required if there is significant acccumulation in fish of the active ingredient and/or its principal degradation products.

(12) Not required if the active ingredient or any of its hydrolytic products do not show absorption or tailing between 290 and 800 Fm.

158.1116 Application exposure monitoring data requirements.

158.1117 General requirements.

(a) Monitoring data are required to assess exposure and resulting risk to those individuals who handle antimicrobial pesticides or are involved in tasks related to their use. These data are used to determine if an antimicrobial pesticide can be safely used given the range of protective measures (clothing and/or equipment) which are available to protect those individuals involved in pesticide application.

(b) The purpose of data required is to measure potential dermal and respiratory exposure to pesticides when used according to widespread and commonly recognized practice. Individuals who have contact with antimicrobial pesticides in the course of their work activities will be exposed to pesticide chemicals through different routes and to a different extent than the general population. Data required may include dermal exposure, inhalation exposure, biological monitoring,or detailed use information. Use information pertains to the mkethods of mixing, loading and application of pesticides and associated cultural practices and will play an integral part in determining exposure to antimicrobial pesticide handlers.

(c) These requirements address direct exposure encountered during any pesticide application operation and related occupational activities including weighing and mixing the concentrated chemical or loading the material into the application equipment. In estimating exposure, pertinent use information is considered along with estimates of the frequency and duration of each application activity under consideration. The estimated exposure for the required time interval (daily and annually depending on whether the assessment is for an acute or chronic toxicological concern) is considered along with the results of biological effects studies to produce a quantitative risk assessment.

(d) Workplace standards for many industries are set by the Occupational Safety and Health Agency (OSHA). If EPA determines that industrial standards provide adequate protection for an antimicrobial pesticide, e.g., the active ingredient in antifouling paint, monitoring for that use would not be required.

158.1118 Data requirements for application exposure monitoring.

(a) Table. Section 158.1104 describes how to use the table to determine the application exposure monitoring data requirements and the substances to be tested. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (b) of this section, and apply to the individual tests when referenced in the following table.

Table 1. Human exposure data requirements - application.

Data Requirements	Agricultural	Food handling	Commercial	Residential	Medical	Human drinking water	Test Substance	Guideline Reference	
								Old	New
Application									
Product use information	R	R	R	R	R	R	TEP	none	875.1700
Dermal exposure outdoor	CR 1		CR 1	CR 1		R 4	TEP	231	875.1100, 875.1600
Dermal exposure indoor	R	R	R	R	R	R 4	TEP	233	875.1200, 875.1600
Inhalation exposure outdoor	CR 1		CR 1	CR 1		R 4	TEP	232	875.1300, 875.1600
Inhalation exposure indoor	R	R	R	R	R	R 4	TEP	234	875.1400, 875.1600
Biological monitoring	CR 2	CR 2	CR 2	CR 2	CR 2	CR 2	TEP	235	875.1500, 875.1600

Data Requirements	Materials preservatives	Industrial processes	Antifouling coating	Wood pre-servatives	Swimming pools	Aquatic areas	Test Substance	Guideline Reference	
								Old	New
Application									
Product use information	R	R	R	R	R	R	TEP	none	875.1700
Dermal exposure outdoor	CR 1	CR 1	CR 1	R 3	CR 1	R	TEP	231	875.1100, 875.1600
Dermal exposure indoor	R	R	R	R 3	R	CR 5	TEP	233	875.1200, 875.1600
Inhalation exposure outdoor	CR 1	CR 1	CR 1	R 3	CR 1	R	TEP	232	875.1300, 875.1600
Inhalation exposure indoor	R	R	R	R 3	R	CR 5	TEP	234	875.1400, 875.1600
Biological monitoring	CR 2	CR 2	CR 2	CR 2	CR 2	CR 2	TEP	235	875.1500, 875.1600

(b) Test notes.

(1) Required for outdoor uses only if such uses are outdoor or outdoor uses are expected to result in greater exposure than indoor use.

(2) Biological monitoring may be submitted in addition to or instead of dermal/inhalation exposure data provided adequate pharmacokinetics data are available to interpret the biological monitoring data.

(3) Required to evaluate exposure of handlers for each intended preservation use pattern: 1)joinery; 2) pressure treatment; 3) remedial; 4) sapstain; and 5) Ready-to-Use.

(4) Not required if antimicrobial agent is applied in closed loading and application systems.

(5) Required for indoor uses such as aquaria only if such uses are expected to result in greater exposure than outdoor use.

158.1119 Post-application exposure monitoring data requirements.

(a) General requirements. These data are required to assess risk resulting from post-application exposure to pesticides. Evaluation of these risks are derived from studies on toxicity, residue dissipation, and human exposure. Monitoring data generated during the exposure studies are used to determine the quantity of pesticide to which people may be exposed after application and to develop reentry intervals where applicable (agricultural/industrial sites) or evaluate whether a product may be used safely in residential sites.

(b) Workplace standards for many industries are set by the Occupational Safety and Health Agency (OSHA). If EPA determines that industrial standards provide adequate protection for an antimicrobial pesticide, e.g., the active ingredient in antifouling paint, monitoring for that use would not be required.

158.1120 Data requirements for post-application exposure monitoring.

(a) Table. Section 158.1104 describes how to use this table to determine the post-application exposure monitoring data requirements and the substance to be tested. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (b) of this section, and apply to the individual tests when referenced in the following table.

Table 1. Human exposure data requirements - post-application.

Data Requirements	Agricultural	Food handling	Commercial	Residential	Medical	Human drinking water	Test Substance	Guideline Reference	
								Old	New
Post-application									
Description of human activity	R	R	R	R	R		TEP	133-1	875.2800
Indoor surface residue dissipation	CR 1	CR 1	CR 1	R 1	R 5		TEP	none	875.2300, 875.2900
Dermal exposure	CR 2	CR 4	CR 2	R 2	R 2		TEP	133-3	875.2400, 875.2900
Inhalation exposure	CR 2	CR 4	CR 2	R 2	R 2		TEP	133-4	875.2500, 875.2900
Biological monitoring	CR 3	CR 3	CR 3	CR 3	CR 3		TEP	235	875.2600, 875.2900

Data Requirements	Materials preservatives	Industrial processes	Antifouling coating	Wood pre-servatives	Swimming pools	Aquatic areas	Test Substance	Guideline Reference	
								Old	New
Post-application									
Product use information	R	R	R	R	R	R	TEP	none	875.2700
Description of human activity	R	R	R	R	R	R	TEP	133-1	875.2800
Indoor surface residue dissipation	R 1	CR 1		R 5			TEP	none	875.2300, 875.2900
Dermal exposure	R 2	CR 2	R 7	R 6			TEP	133-3	875.2400, 875.2900
Inhalation exposure	R 2	CR 2	R 7	R 6		CR 9	TEP	133-4	875.2500, 875.2900
Biological monitoring	CR 3	CR 3	CR 3	CR 3	CR 8	CR 3	TEP	235	875.2600, 875.2900

(b) Test notes.

(1) Required if the use pattern and formulation types involve significant potential exposure to humans by contact with residues on treated surfaces.

(2) Testing for post-application exposure would be needed unless the product use information and description of human activity, or chemical characteristics of the products in this category, indicate that exposure in and near areas where the pesticide has been applied is not likely to be significant.

(3) Biological monitoring may be submitted in addition to or instead of dermal/inhalation exposure data provided adequate pharmacokinetics data are available to interpret the biological monitoring data.

(4) Testing would be required for all uses expected to result in exposure to significant populations or at levels like to pose significant risk.

(5) If the use pattern and formulation types involve significant potential exposure to humans by evaporation of residues from surfaces or contact with residues on treated surfaces, the surface residue study may be required in addition to dermal/inhalation data.

(6) Testing for post-application exposure is required to: (1) evaluate exposure to persons removing antifouling coatings from treated surfaces, such as boat hulls, if the activity is not covered by OSHA regulations, and (2) evaluate bystander inhalation exposure following application of antifouling coatings.

(7) Required to evaluate exposure of for each intended preservation use pattern: 1)joinery;
2) pressure treatment; 3) remedial; 4) sapstain; and 5) Ready-to-Use.

(8) Biological monitoring of swimmers required if estimated risk is significant.

(9) For indoor aquaria or ornamental ponds only.

Filename: Subprtw.doc
Directory: C:\MyFiles
Template: C:\WINDOWS\Application Data\Microsoft\Templates\Normal.dot
Title:
Subject:
Author: OPP
Keywords:
Comments:
Creation Date: 06/21/2000 2:41 PM
Change Number: 1
Last Saved On:
Last Saved By:
Total Editing Time: 0 Minutes
Last Printed On: 06/21/2000 2:42 PM
As of Last Complete Printing
Number of Pages: 56
Number of Words: 12,043 (approx.)
Number of Characters: 68,649 (approx.)